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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/802,441	03/16/2004	Daniel McVicar	58581 (47992)	4032

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EXAMINER	
HADDAD, MAHER M	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 11/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/802,441	MCVICAR ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-53* is/are pending in the application.

4a) Of the above claim(s) *1-34,36,37, 40, 43-46, 49 and 51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35,38,39,41,42,47,48,50,52 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-53 are pending.

2. Applicant's election with traverse of Group XXIII, claims 35, 38-48 and 50 (now claims 35, 38-39, 42, 48, 50 and 52-53), drawn to a method for treating a subject having a disorder comprising administering to the subject a TLT-1 modulator, wherein the TLT-1modulator is an antibody that selectively binds TLT-1, wherein the disorder is clotting disorders or bleeding disorders and SEQ ID NO: 17 as the species filed on 8/18/06, is acknowledged.

Applicant's traversal is on the grounds that multiple groups as defined in the Office action can be considered at this time without undue burden. Applicant submits that Groups XII-XXV have the same classification at both the class and subclass levels. Accordingly, Applicant concludes that multiple groups can be considered together at this time. This is not found persuasive because as stated in the previous Office Action that even though in some cases the classification is shared, a different field of search would be required based upon the structurally distinct products recited and the various methods of use comprising distinct method steps. Further, a prior art search also requires a literature search. It is an undue burden for the examiner to search more than one invention. Therefore the methods of treating various disorders with an antibody to TLT-1 or TLT-1 polypeptide are distinct and independent, and searches of all groups would place an undue burden upon the examiner due to the distinct and divergent subject matter of each Group. Further, a prior art search also requires a literature search. It is an undue burden for the examiner to search more than one invention.

The requirement is still deemed proper and is therefore made FINAL.

Upon reconsideration the Examiner has extended the search to cover SEQ ID NO:5.

3. Claims 1-34, 36, 49 and 51 (non- elected Groups) and 40, 43-46 (non-elected species) are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

4. Claims 35, 38-39, 41-42, 47-48, 50 and 52-53 are under examination as they read on a method for treating a subject having a disorder comprising administering to the subject a TLT-1 modulator, wherein the TLT-1modulator is an antibody that selectively binds TLT-1, wherein the disorder is clotting disorders or bleeding disorders and SEQ ID NO: 17 and 5 as the species.

5. Applicant's IDS, filed 8/26/05, is acknowledged.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 35, 38-39, 41-42, 47-48, 50 and 52-53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not reasonably provide enablement for a method for treating a subject having a "clotting disorders or bleeding disorders" comprising administering to the subject a therapeutically effective amount of a "TLT-1 modulator" in claim 35, wherein the TLT-1 modulator is an antibody that selectively binds to TLT-1 in claim 38 and 52, wherein the antibody binds to a TLT-1 polypeptide that "can modulate platelet function" in claim 39, Wherein the antibody binds to a polypeptide comprising the amino acid sequence of SEQ ID NO:17 in claim 42, wherein the a monoclonal antibody is administered to the subject in claim 48, wherein the subject is suffering from a "clotting disorder or bleeding disorder" in claim 50, wherein the subject is suffering from a clotting disorder in claim 53. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Since no animal model system are used to treat a subject having clotting disorders or bleeding disorders, and *in vitro* studies have not correlated well within vivo clinical trial results in patients. Since the method of treating clotting disorders or bleeding disorders indices of administering to the subject an antibody that selectively binds to TLT-1 can be species- and model-dependent, it is not clear that reliance on the *in vitro* studies accurately reflects the relative human efficacy of the claimed treatment strategy. The specification does not adequately teach how to effectively treat of clotting or bleeding disorders or reach any treatment endpoint in any subject including humans by administering modified an anti-TLT-1 antibody. The specification does not teach how to extrapolate data obtained from in vitro studies to the development of effective in vivo treatment in a subject including human, commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of the anti-TLT-1 antibodies

exemplified in the specification.

At issue is the treatment of "clotting disorders or bleeding disorders" with the same anti-TLT-1 antibodies. The skilled artisan would not know what disorder to treat with the same anti-TLT-1 antibodies, clotting disorders (inhibition of bleeding) such as ischemia and/or infarction, including stroke and heart attack or bleeding disorders (induction of blood clotting) such as Hemophilia. The specification fails to provide guidance as to how to modulate bleeding with the same anti-TLT-1 antibodies. It is unclear whether such a desired effect can be achieved or predicted, as encompassed by the claims. In order to "modulate" bleeding, the process requires inhibiting and activating antibodies. Said antibodies are mutually exclusive in that they reach opposing endpoints, and in that they employ structurally distinct agonists or antagonists to accomplish these mutually exclusive endpoints. Thus, faced with contradictory and seemingly mutually exclusive function regarding the activity of the claimed antibody, undue experimentation would be required of the skilled artisan to determine the effect of anti-TLT-1 antibodies on platelets activity. Further, absent the ability to predict which of these antibodies would function as claimed, for one of skill in the art to practice the invention as claimed would require a level of experimentation that is excessive and undue.

Due to the contradictory and seemingly mutually exclusive activity of the anti-TLT-1 antibodies, undue experimentation would be required of the skilled artisan to determine the effect of TLT-1 on any particular disorder in view of the instant disclosure. Further, there is insufficient evidence or nexus that would lead the skilled artisan to predict the ability of TLT-1 antibodies to treat clotting or bleeding disorders. Even the capability of TLT-1 polypeptide to up-regulate on the blood platelets surface after activation alone does not indicate that TLT-1 play role in the adhesion of activated platelets to endothelium or one another (see page 87, lines 18-20 of the specification). Gattis et al (JBC, 281:13396-13403, 2006) teach that a soluble fragment of the TLT-1 extracellular domain is found in serum of humans and mice and that an isoform of similar mass is released from platelets following activation wit thrombin (see abstract in particular). Importantly, Gattis et al conclude that this immunoglobulin-like domain autonomously plays and as yet unidentified, functional role (see abstract). The target ligand of TLT-1 Ig-like domain is not yet identified. TLT-1 function on platelets is not yet established. Applicant's strategy to enhance clot formation/clot retraction using anti-TLT-1 antibodies is fraught with inaccuracies and that these methods are still notably deficient in defining and describing the complexity of TLT-1 function in platelet activity.

The exemplification in the specification is demonstrate that stimulation of platelets with thrombin or collagen dramatically up-regulates surface expression of TLT-1 polypeptide. While such *in vitro* assay may provide an indication that particular compounds/compositions are appropriate to target for *further experimental consideration.* Applicant's disclosure does not appear to have provided the skilled artisan with sufficient guidance and support as how to extrapolate data obtained from *in vitro* assay to the development of effective *in vivo* human therapeutic methods, commensurate in scope with the claimed invention.

On the basis of the disclosed correlation of the surface up-regulation of TLT-1 polypeptide in

activated platelets observation alone, applicant concludes that the scope of the antibody against TLT-1encompassed by the claimed invention can have biological activity to treat clotting disorders or bleeding disorders and be provided as pharmaceutical compositions to subjects including human to effectively clotting disorders or bleeding disorders. It cannot be seen how the same anti-TLT-1 antibodies can be used to treat clotting disorders or bleeding disorder. Although such antibodies were to induce clot formation in a subject, it is unclear how the same antibodies would participate in clot retraction.

Finally, the term "comprising" in the 42 and 47 is open-ended it would open up the claimed sequences to include unspecified amino acid on either or both of the N- and C- terminal of the claimed sequences.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

8. Claims 35, 38-39, 41-42, 47-48, 50 and 52-53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is not in possession of a method for treating a subject having a "clotting disorders or bleeding disorders" comprising administering to the subject a therapeutically effective amount of a "TLT-1 modulator" in claim 35, wherein the TLT-1 modulator is an antibody that selectively binds to TLT-1 in claim 38 and 52, wherein the antibody binds to a TLT-1 polypeptide that "can modulate platelet function" in claim 39, Wherein the antibody binds to a polypeptide comprising the amino acid sequence of SEQ ID NO:17 in claim 42, wherein the a monoclonal antibody is administered to the subject in claim 48, wherein the subject is suffering from a "clotting disorder or bleeding disorder" in claim 50, wherein the subject is suffering from a clotting disorder in claim 53.

Neither the exemplary embodiments nor the specification's general method appears to describe structural features, in structural terms, that are common to the genus. That is, the specification provides neither a representative number of species (TLT-1 modulator) to describe the claimed genus, nor does it provide a description of structural features that are common to species (TLT-1 modulator). As discussed above, the specification provides no structural description of TLT-1 modulator other than ones specifically exemplified; in essence, the specification simply directs those skilled in the art to go figure out for themselves what the claimed TLT-1 modulator looks like. The specification's disclosure is inadequate to describe the claimed genus of TLT-1 modulator.

Applicant has disclosed only amino acid of SEQ ID NO: 2, 5, 17, 19, 22, 25, ; therefore, the skilled artisan cannot envision all the contemplated TLT-1 modulator possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

35 U.S.C. § 102(e), as revised by the AIPA and H.R. 2215, applies to all qualifying references, except when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. For such patents, the prior art date is determined under 35 U.S.C. § 102(e) as it existed prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. § 102(e)).

10. Claims 35, 38-39, 41-42, 47-48, 50 and 52-53 are rejected under 35 U.S.C. 102(a)/(e) as being anticipated by WO 03/020005 A2.

The `005 publication teaches a method of treating heart attack and stroke (clotting disorders) and aiding in recovery after heart transplantation (bleeding disorder) with antibody to LP357 polypeptide (see page 81, lines 26-34 in particular). LP357 polypeptide comprising the amino acid sequence 2-16 of SEQ ID NO:17 at positions 228-242 of LP357 sequence (see referenced SEQ ID NO: 4 and page 76 in particular). Further, the referenced LP357 is 100% identical to claimed SEQ ID NO:5.

The reference teachings anticipate the claimed invention.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

October 18, 2006

Maher Haddad

Maher Haddad, Ph.D.
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